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# Inverse Problem of Electrocardiography: estimating the location of cardiac ischemia in a 3D geometry

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**Abstract.** The inverse problem in cardiology (IPC) has been formulated in different ways in order to non invasively obtain valuable informations about the heart condition. Most of the formulations solve the IPC under a quasistatic assumption neglecting the dynamic behavior of the electrical wave propagation in the heart. In this work we take into account this dynamic behavior by constraining the cost function with the monodomain model. We use an iterative algorithm combined with a level set formulation allowing us to localize an ischemic region in the heart. The method has been presented by Alvarez et al in [1] and [4], in which the authors developed a method for localize ischemic regions using a simple phenomenological model in a 2D cardiac tissue. In this work, we analyze the performance of this method in different 3D geometries. The inverse procedure exploits the spatiotemporal correlations contained in the observed data, which is formulated as a parametric adjust of a mathematical model that minimizes the misfit between the simulated and the observed data. We start by testing this method on two concentric spheres and then analyze the performance in a 3D real anatomical geometry. Both for analytical and real life geometries, numerical results show that using this algorithm we are capable of identifying the position and, in most of the cases, approximate the size of the ischemic regions.

## 1 Introduction

Cardiac arrhythmias are disturbances in the normal rhythm of the heart produced by an abnormal electrical activity. They are one of the major causes of death worldwide [19]. Cardiac arrhythmias can be analyzed by means of non-invasive procedures aiming to characterize the cardiac electric sources (membrane potential, epicardial or endocardial potentials, activation times) and/or the cardiac substrate (ischemia regions, post-infarct scars) from voltages recorded by electrodes systems which are not in direct contact with the cardiac tissue [17,

2]. From a mathematical point of view, the problem of recovering the heart electrical activity from remote voltages can be formulated as an inverse problem, known as the inverse problem of electrocardiography (IPE) [8]. The IPE is a hard technological challenge since in its general formulation is an ill-posed problem so a number of regularization approaches have been developed over the years to obtain stable and realistic solutions [9, 7, 3].

In the present study we analyze the IPE in terms of localizing cardiac ischemic regions from remote voltage measurements. Cardiac ischemia is a pathology produced by the lack of blood supplied to the heart muscle that generates electrophysiologically-abnormal substrate which may lead to life threatening arrhythmias, and ultimately to a heart attack [10]. In the clinical practice, determining the size and location of cardiac ischemic regions has shown limited accuracy, specially in severe damaged hearts [20]. Ischemia alters the propagation properties of the electrical impulse through the cardiac muscle and this results in alterations in the associated voltage measurement recordings. These alteration patterns are temporally stable, making it feasible to inversely reconstruct ischemic regions from voltage measurements recordings [21].

Previous works have analyzed the localization of cardiac ischemia from remote voltage measurements [21, 11, 12, 5, 1]. In [11, 5] the size and position of myocardial infarction is estimated by minimizing the difference between real voltage measurements and model-simulated ones. In [12, 18, 15] ischemic regions are assessed by reconstructing the epicardial potentials at a single time-instant during the plateau phase of the cardiac membrane potential by using a level-set formulation. Wang et al. [21] formulated the IPE as a constraint minimization problem, in which the the size and position of ischemic regions were estimated by inversely computing the membrane potential at a single time instant during the plateau phase. While showing promising results towards clinical validation [21, 15], in these studies time instants are treated independently from the others, thus ignoring the spatiotemporal correlation information contained in the voltage measurements. On the other hand, Álvarez et al. [1] presented an algorithm being able to reconstruct disconnected cardiac ischemic regions with a limited number of recording sites by exploiting the spatiotemporal correlation contained in the measured data.

Here, we extend the work presented in [1] to 3D geometries. We analyze the performance of the method in a model of spheres and then we study its use on 3D realistic anatomical model. Our results show that the algorithm is capable of identifying the position and, in most of the cases, approximates the size of the ischemic regions.

## 2 Forward Calculation

The forward problem refers to the mathematical models that describes the ionic processes involved in the generation of the action potential, its propagation through the cardiac tissue and remote recording model. In this section, we present the models used for the forward simulations.

### 2.1 Action potential model

Cellular electrical activity was simulated using a modified version of the Two-Current model (TC), proposed by Mitchell and Schaeffer [14]. The TC consists

of just two ordinary differential equations for two variables: the transmembrane potential or voltage  $v(t)$  and the inactivation gate variable  $h(t)$ . The voltage, which is dimensionless and scaled so that it varies between zero and one is defined as follows

$$\frac{dv}{dt} = J_{TC} = J_{stim}(t) + J_{in}(v, h) + J_{out}(v), \quad (1)$$

where  $J_{stim}$  represents the initial stimulus,  $J_{in}$  and  $J_{out}$  denotes the sum of all inward and outward currents, respectively. In order to simulate ischemia, we incorporated a parameter ( $v_{rest}$ ) associated to the resting potential formulated by Alvarez et al [1],

$$J_{in}(v, h) = \frac{h(1-v)(v-v_{rest})^2}{\tau_{in}}, \quad (2)$$

$$J_{out}(v, h) = -\frac{v-v_{rest}}{\tau_{out}}. \quad (3)$$

The gating variable  $h(t)$  is dimensionless and varies between zero and one. This variable regulates inward current flows and obeys the following equation

$$\frac{dh}{dt} = G(v, h) = \begin{cases} (1-h)/\tau_{open}, & v < v_{crit} \\ -h/\tau_{close}, & v \geq v_{crit} \end{cases} \quad (4)$$

This model contains four time constants ( $\tau_{in}$ ,  $\tau_{out}$ ,  $\tau_{open}$  and  $\tau_{close}$ ) which correspond to the four phases of the cardiac action potential: initiation, plateau, decay and recovery. The parameter  $v_{crit}$  is the change-over voltage. We simulate the effects of ischemia modifying the values of  $\tau_{in}$  and  $v_{rest}$  [4]. For ischemic cells, we set the parameter  $\tau_{in}$  and  $v_{rest}$  equal to 0.8 and 0.1, respectively.

## 2.2 Cardiac Tissue Model

The monodomain equation was used to simulate the electrical activity of the heart. Despite the discrete nature of cardiac cells structure, at the macroscopic scale cardiac tissue behaves as a functional syncytium. This permits to consider cardiac tissue ( $\Omega_H$ ) as an excitable medium in which the membrane potential propagation can be mathematically described according to the following reaction-diffusion equation

$$\frac{\partial v}{\partial t} = \nabla \cdot (D \nabla v(\mathbf{r}_H, t)) + J_{TC} \quad (5)$$

where  $D$  is the intracellular conductivity tensor, which is set to a constant value of  $D = 1.4 \text{ mm}^2/\text{ms}$ . Imposing  $v(\mathbf{r}_H, 0) = v_{rest}$  and  $h(\mathbf{r}_H, 0) = 1$  as initial conditions and no-flux boundary conditions.  $J_{TC}$  is taken as the ion current provided by TC model.

## 2.3 Remote Recording Model

The resulting potential distribution at position  $\mathbf{r}_T = (x_T, y_T, z_T) \in \Omega_T$  outside the cardiac tissue  $\Omega_H$ , is found by the addition (volume conductor theory) of the contribution of all source elements [13, 16]. In this work, we consider remote recording measurements modeled as point electrodes at a distance  $R(\mathbf{r}_H - \mathbf{r}_T) =$

$\|\mathbf{r}_T - \mathbf{r}_H\|$  from source location  $\mathbf{r}_H = (x_H, y_H, z_H) \in \Omega_H$  to observation point  $\mathbf{r}_T^i$  given by

$$\varphi^i(\mathbf{r}_T^i, t) = \frac{1}{4\pi\sigma_0} \int_{\Omega_H} \frac{\nabla \cdot (D\nabla v(\mathbf{r}_H, t))}{R(\mathbf{r}_H, \mathbf{r}_T^i)} d\Omega_H \quad (6)$$

where  $\sigma_0$  represents the medium conductivity (assumed homogeneous), and  $v(\mathbf{r}_H, t)$  is solution of (5). Expressions (1)-(6) comprise a complete description of the forward problem.

### 3 Inverse Procedure

The aim of the inverse procedure is to estimate the shape and locations of the ischemic areas adjusting the parameter distribution of  $\tau_{in}$  and  $v_{rest}$  from the knowledge of the remote recordings measurements  $\varphi^i(\mathbf{r}_T, t)$ . The functional to be minimized is the  $L^2$  norm of the misfit between the observed data and the simulated torso measurement,  $\varphi_R^i(\mathbf{r}_T^i, t)$  and  $\varphi_S^i(\mathbf{r}_T^i, t)$  respectively:

$$\begin{aligned} \mathcal{J}(\tau_{in}(\mathbf{r}_H), v_{rest}(\mathbf{r}_H)) &= \frac{1}{2} \int_0^T \sum_{i=1}^N \left\| \varphi_R^i(\mathbf{r}_T^i, t) - \varphi_S^i(\mathbf{r}_T^i, t; \tau_{in}, v_{rest}) \right\|^2 dt \\ &= \frac{1}{2} \int_0^T \sum_{i=1}^N \left\| \varphi_R^i(\mathbf{r}_T^i, t) - \left\{ \frac{1}{4\pi\sigma_0} \int_{\Omega_H} \frac{\nabla \cdot (D\nabla v(\mathbf{r}_H, t))}{R(\mathbf{r}_H, \mathbf{r}_T^i)} d\Omega_H \right\} \right\|^2 dt \end{aligned} \quad (7)$$

where  $T$  represents the recording time and  $N$  the number of electrodes.

In this approach, we follow an iterative scheme in which the cost functional is reduced at each step ( $\xi$ ) of the reconstruction process. Therefore, we find a direction in the space parameter  $(\tau_{in}(\mathbf{r}_H), v_{rest}(\mathbf{r}_H))$  such that the cost functional decreases. Since both parameters,  $\tau_{in}(\mathbf{r}_H)$  and  $v_{rest}(\mathbf{r}_H)$ , define the same region, we only consider the variation of  $\tau_{in}(\mathbf{r}_H)$  for the gradient computation. The ischemic region is defined by a level set function as in [1]. Subsequently, as we change the parameter distribution of  $\tau_{in}(\mathbf{r}_H)$ , distribution of  $v_{rest}(\mathbf{r}_H)$  is modified as well. Following [1], the gradient of the function  $\mathcal{J}$  over the parameter  $\tau_{in}$  is given by

$$grad_{\tau_{in}} \mathcal{J}(\tau_{in}(\mathbf{r}_H)) = \int_0^T w(\mathbf{r}_H, t) \frac{h(\mathbf{r}_H, t) [v(\mathbf{r}_H, t) - v_{rest}(\mathbf{r}_H)]^2 [v(\mathbf{r}_H, t) - 1]}{\tau_{in}^2(\mathbf{r}_H)} dt \quad (8)$$

where adjoint state  $w$  is the solution of the following problem

$$\begin{cases} \frac{\partial w}{\partial t} + \nabla D \cdot \nabla w(\mathbf{r}_H, t) - \frac{\partial J_{TC}}{\partial \tau_{in}} w(\mathbf{r}_H, t) = -\frac{1}{4\pi\sigma_0} \sum_{i=1}^N \mathcal{R}_i \left[ \int_{\Omega_H} \nabla^2 \left( \frac{1}{R(\mathbf{r}_H, \mathbf{r}_T^i)} \right) d\Omega_H \right] dt \\ w(\mathbf{r}_H, t = T) = 0 \end{cases} \quad (9)$$

where  $\mathcal{R}_i = \|\varphi_R^i(\mathbf{r}_T^i, t) - \varphi_S^i(\mathbf{r}_T^i, t)\|$ , and

$$\frac{\partial J_{TC}}{\partial \tau_{in}} = \left\{ \frac{h(\mathbf{r}_H, t) - v_{rest}(\mathbf{r}_H)}{\tau_{in}(\mathbf{r}_H)} (2 - 3v(\mathbf{r}_H, t) + v_{rest}(\mathbf{r}_H)) - \frac{1}{\tau_{out}(\mathbf{r}_H)} \right\}. \quad (10)$$

## 4 Numerical Experiments and Results

In this section, we present some numerical experiments in order to analyze the behavior of the inverse algorithm on 3D geometries. We conducted two scenarios: (1) initialize the method with different initial guesses using a two concentric spheres geometry, (2) study the performance of the algorithm in a real anatomical geometry. For all experiments, the reconstruction algorithm is applied to a single cardiac cycle of length  $T = 240$  ms in the steady state. The inverse procedure stops when the functional cost becomes stationary.

### 4.1 First Experiment

**Simulation Setup.** For the first scenario, we consider a spherical cardiac tissue of radius 50.0mm which might contain one or several ischemic regions. The cardiac tissue domain,  $\Omega_H$ , was discretized by a triangular finite element mesh generated with Gmsh [6]. For the remote measurement points  $\Omega_T$ , we set a concentric sphere of radius 65.0mm.

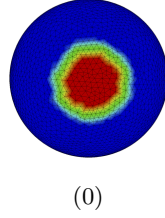
**Scenario.** We suppose a circular ischemic region of radius 14 mm as is shown in Figure 1 panel (0). The aim of this experiment is to verify if the inverse procedure is able to reconstruct a single ischemia independently of the initial guess. We simulated three different cases: (a) supposing a healthy cardiac tissue i.e., there is not an ischemic region, (b) initialize the method with a ischemic region close to the real position and (c) considering an ischemic region elsewhere in the cardiac tissue (see Figure 1 panel (a1), (b1) and (c1), respectively). Figure 1 panel (a2), (b2) and (c2) shows reconstructed  $\tau_{in}$  for each case, respectively. A qualitative comparison between the obtained reconstruction and the real ischemic region shows that position and size of the ischemia was reconstructed successfully for all cases. We have computed the correlation coefficient between the true ischemia distribution and the distribution obtained from the inverse problem. For all cases, the correlation coefficient (CC) excess a value of 0.95 ( $CC1 = 0.9571$ ,  $CC2 = 0.9543$  and  $CC3 = 0.9532$ ) which is consistent with the reconstructions observed in Figure 1.

### 4.2 Second Experiment

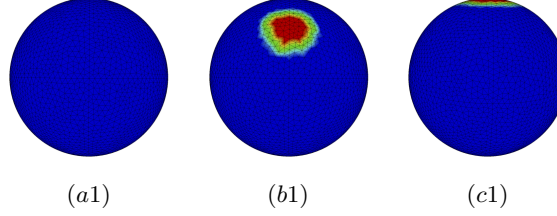
**Anatomical model** As a geometry, we use a 3D mesh of torso and heart obtained from a CT scan of a 43 years old woman (Figure 2 panel (a)). We used the medical imaging software Osirix to segment the heart and the torso from the CT scan DICOM files. We then construct the meshes using the CardioViz3D software.

**Scenario.** We suppose a circular ischemic region of radius 13 mm as is shown in Figure 2 panel (a). Contrary to the methodology used in Alvarez et al [1], for this experiment we do not assume an ischemic initial guess. We start the iterative method assuming healthy conditions for the entire tissue. At each iteration, the functional cost gradient is computed and both parameters,  $\tau_{in}$  and  $v_{rest}$ , are updated. After 28 iterations, stop criteria is accomplished obtaining the final reconstruction. For this scenario, we obtain a correlation coefficient between the reconstructed ischemic region and the ground truth of  $CC = 0.8241$ .

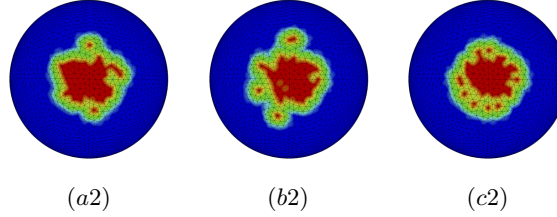
### Real Ischemia



### Initial Guess



### Reconstruction

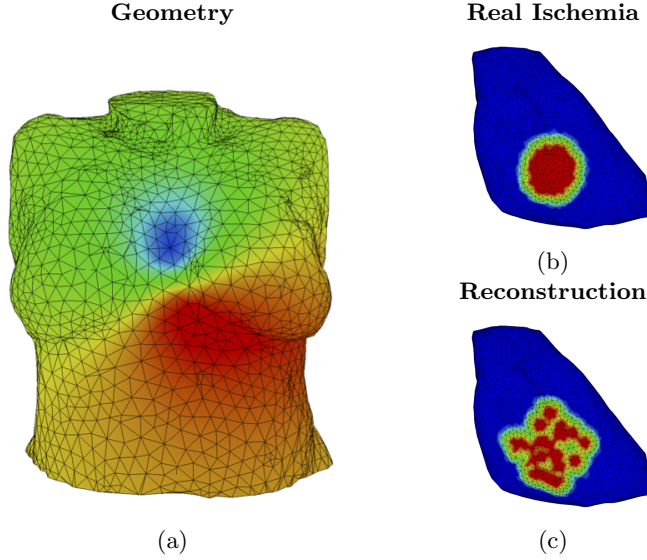


**Fig. 1.** First row: The image represents the spatial distribution of the ischemia: red ischemia, green border zone and blue health tissue. Second row represents initial guesses ( $\tau_{in}$  configuration) for different simulation cases. Case (a): a healthy cardiac tissue, Case (b): initializing with a small ischemic region close to the real one and Case (c): considering an ischemic region elsewhere in the cardiac tissue. Third row shows the final reconstruction of the ischemic region

## 5 Discussion and Conclusions

In literature, we can find different methodologies to address the problem of localize ischemic regions using potential measurements taken at the body surface. Many of them use voltage measurements in an instant of time, without taking into account the spatio-temporal correlation presented in EGM measures. In this paper, we used the method proposed by [1] and tested on 2D geometries in order to reconstruct ischemic areas. This algorithm allows to solve the inverse problem including, into the formulation of level set, a regularization with the spatio-temporal correlation presented in the recordings.

The methodology was tested on different 3D geometries. First, the correct performance of the method was tested in a two concentric spheres geometry. Where it was found that the solution to this problem is not dependent on the initial guess for the inverse procedure. Subsequently, we analyze the behavior to a more realistic geometry. We solved the inverse problem considering a single ischemia in a real anatomical geometry. The quality of the results obtained for



**Fig. 2.** Second Experiment: (a) A snapshot of the torso potential at time 170 ms. (b): Representations of the true ischemic region ( $\tau_{in}$  configuration). (c): The reconstructed ischemia region.

each of the proposed scenarios shows that the ischemic region has been located satisfactorily, obtaining a correlation coefficient exceeds the value of 0.95 for the spheres scenario and for the anatomical geometry is around 0.85. We think that this difference in the CC is due to the fact that the torso surface in the spherical case is much closer to the heart surface than it is for the anatomical geometry.

In future work, we aim to incorporate more realistic settings using an electrophysiology detailed model, with a physiological representation of the ischemia model. We will also investigate the performance of this method in localizing ischemia from clinical measurements. This assumes that the electrophysiological model that would be used to constrain the minimization problem is sufficiently accurate.

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